initial or second-line antihypertensive therapy, separating amlodipine from other calcium antagonists. The results were:

Event	Fixed-Effects Meta-analyses		Network Meta-analyses	
	Summary Odds Ratio (95% CI)	P(homo)	Odds Ratio (95% CI, vs. Diuretic)	ω
Death	0.94 (0.90-0.99)	0.79	0.96 (0.91-1.01)	0.0000001
CV Death	0.91 (0.84-0.98)	0.02	0.98 (0.90-1.06)	0.0000001
Stroke	0.84 (0.78-0.90)	0.16	0.92 (0.83-1.02)	0.000001
CHD	0.92 (0.87-0.98)	0.04	0.88 (0.77-1.00)	0.00001
MACE	0.89 (0.86-0.94)	0.001	0.92 (0.86-0.99)	0.06
HF	1.23 (1.16-1.33)	0.001	1.38 (1.25-1.54)	0.02

CI = confidence interval; CV = cardiovascular; CHD = coronary heart disease; MACE = major adverse CV events (stroke, CHD, CV death; estimated for some trials); HF = heart failure.

These data suggest that, in clinical trials, amlodipine significantly increased the risk of heart failure, but prevented other cardiovascular endpoints at least as well as other regimens, including those that started with a diuretic.

Keywords: Meta-analysis; Inhomogeneity; Heart failure; Network

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Effects of perindopril on cardiovascular outcomes in hypertension clinical trials: traditional and network meta-analyses

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Although the FDA has approved a statement that ''lowering blood pressure reduces the risk of adverse cardiovascular outcomes,'' only a few individual antihypertensive agents have been used in outcomes-based clinical trials, typically against several different comparators. To estimate the cardiovascular effects of perindopril, traditional, fixed-effects meta-analyses were performed, using data from 5 clinical trials (EUROPA, PROGRESS, ADVANCE, HYVET, ASCOT) involving 26,302 subjects who were randomized to receive perindopril as part of their drug regimen, compared to 26,263 randomized to another regimen. In an attempt to identify and minimize inhomogeneity among all comparators, network meta-analyses were also performed, using data from 86 trials that randomized 433,705 subjects, separating perindopril from other ACE-inhibitors. The results were:

Event	Fixed-Effects Meta-Analyses	P(homo)	Network Meta-Analyses	ω
	Summary Odds Ratio (95% CI)		Odds Ratio (95% CI, vs. Diuretic)	
Death	0.88 (0.82-0.93)	0.76	0.94 (0.85-1.03)	0.03
CV Death	0.82 (0.75-0.90)	0.73	0.95 (0.82-1.10)	0.04
Stroke	0.80 (0.73-0.87)	0.05	1.08 (0.89-1.31)	0.07
CHD	0.85 (0.77-0.90)	0.32	0.92 (0.79-1.07)	0.00001
MACE	0.82 (0.77-0.86)	0.06	0.97 (0.86-1.09)	0.04
HF	0.68 (0.58-0.82)	0.01	0.93 (0.75-1.17)	0.000001

CI = confidence interval; CV = cardiovascular; CHD = coronary heart disease; MACE = major adverse CV events (stroke, CHD, CV death; estimated in some trials); HF = heart failure.

These data suggest that, in clinical trials, perindopril significantly prevented all cardiovascular endpoints better than regimens to which it was directly compared (i.e., placebo in 4 of 5 trials), and at least as well as other active antihypertensive drug regimens, including those that started with a diuretic.

Keywords: ACE-inhibitor; Diuretic; Placebo

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Efficacy and safety of perindopril arginine + amlodipine in hypertension

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The angiotensin converting-enzyme (ACE) inhibitor, perindopril, and the calcium antagonist, amlodipine, have demonstrated cardiovascular benefits in randomized clinical trials. To study the efficacy and safety of a new, more chemically stable formulation of perindopril, a three-arm, prospective, 59-center, randomized clinical trial was performed involving 837 subjects, of whom 820 were included in the intention-to-treat analysis. They had an average baseline seated blood pressure (BP) of 158±12/101±5 mm Hg (mean±standard deviation). For 42 days, subjects (average age 52±10 years, 52% male, 34% black, 20% diabetic) received once-daily: amlodipine 10 mg (n=275), the old erbumine salt of perindopril 16 mg (twice the maximum marketed dose, n=274), or amlodipine 10 mg + the new arginine salt of perindopril 14 mg (the likely maximum marketed dose, n=271). Goal BP was < 140/90 mm Hg, or < 130/80 mm Hg in diabetics, in accordance with JNC 7 guidelines. The results of intention-to-treat analyses were:

	Perindopril	Amlodipine	Perindopril + Amlodipine	P <
⊿ Seated BP (mm Hg)	-13.7/-9.5	-19.3/-13.2	-23.7/-15.7	0.001
# At or below goal BP	71 (26%)	101 (37%)	137 (51%)	0.001
Early discontinuation	32 (12%)	28 (10%)	26 (9%)	0.71
Adverse events	77 (28%)	108 (39%)	86 (31%)	0.02
Pedal edema	1 (0%)	36 (13%)	19 (7%)	0.001

No deaths or significant differences across groups in serum potassium, or rates of serious adverse events or glomerular filtration, were observed. These data suggest that the combination of perindopril and amlodipine reduces BP significantly more than either agent alone, and produces significantly less pedal edema than amlodipine.

Keywords: New Formulation; ACE-inhibitor; Combination Therapy; Edema

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Is blood pressure a reliable marker for cardiovascular disease?

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Background: The level of blood pressure (BP) serves as the sole criterion for the diagnosis of hypertension and as the target for its treatment. The recommendation for pharmacologic therapy when pressure is above a specific threshold is based on population data demonstrating higher risk at higher pressures. This population approach to individual management implies that the blood pressure serves as an adequate surrogate for the vascular disease one is addressing with therapy.

Methods: In order to explore the relationship between resting BP and health of the vasculature and heart, we have analyzed the data from 1816 asymptomatic individuals screened for cardiovascular functional